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Effect of Fagarine on Auricular Fibrillation.*

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In 1932 it was demonstrated that an alkaloid from an Argentinian plant, *Fagara coco*, exerts a depressant action on the heart.¹ Subsequent investigations showed that the purified alkaloid, fagarine, raised the fibrillation threshold during faradization of the ventricles² and that it may prevent the fibrillation which follows ligation of the coronary arteries.³

The action of fagarine on the established auricular fibrillation has not been tested because no method was available to elicit this disturbance for a period of sufficient duration without employing other measures which would influence the results. Post-faradization fibrillation is not stable and changes, as a rule, quickly into normal sinus rhythm. Auricular fibrillation persists for a longer time if faradization is combined with the administration of physostigmine, muscarine or choline derivatives. These substances, however, have side-effects on the cardiac muscle which make an evaluation of the experimental results difficult. If, however, 0.05 cc of a 0.05% solution prepared from aconitine crystals is injected subepicardially into the area of the sinus node in dogs it leads to auricular fibrillation or auricular flutter of long duration and permits the study of the effect of rapidly acting drugs. Such attacks of fibrillation occasionally last for more than an hour.⁴

Method. In 10 dogs the chest and the pericardium were opened in the usual way under

nembutal anesthesia and artificial respiration. Both vagi were severed in the neck in 7 experiments. The electrocardiogram was taken in Lead II. After the appearance of persistent auricular flutter or fibrillation 0.004 g/kg of alpha-fagarine chloride was injected intravenously.

Results. In all 10 experiments the flutter or fibrillation disappeared within one minute after the injection ended. Fig. 1a shows auricular fibrillation and its sudden change into sinus rhythm with a rate of 250 following an injection of 0.03 g of fagarine. In Fig. 1b auricular impure flutter changes into a sinus rhythm with a rate of 166. The sinus tachycardia following the disappearance of fibrillation is due at least in part, to the division of the vagi. In those experiments in which the vagi were intact the results were the same.

Table I gives the time intervals between the end of the intravenous injection of fagarine and the disappearance of the prevailing arrhythmia.

Following the injection of fagarine, faradic stimulation of the vagi, even with strong currents, had only a very slight effect on the cardiac rate and on a-v conduction. If larger doses of fagarine are used (0.01/kg) the faradic stimulation of the vagi is without effect.²

Inspection of the exposed heart showed no evidence of dilatation or any disturbance of contractility following the fagarine injection. This should be emphasized because definite dilatation and weakening of cardiac contractions does appear immediately if quinine or quinidine is injected in a dose sufficient to abolish fibrillation. A slight prolongation of the a-v conduction time, amounting to only 0.01-0.02 second appeared at the height of fagarine effect, and the RS-T segments were slightly depressed but no other changes were found in the electrocardiogram. This point

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¹ Stuckert, G., and Sartori, A., *Rev. Univ. Nac. Corboda, Argent.*, 1932, **19**, 12.

² Moisset de Espanes, E., and Moyano Navarro, B., *C. R. Soc. Biol.*, 1938, **127**, 510.

³ Moisset de Espanes, E., *C. R. Soc. Biol.*, 1938, **127**, 233.

⁴ Scherf, D., *Am. Heart J.*, in press.

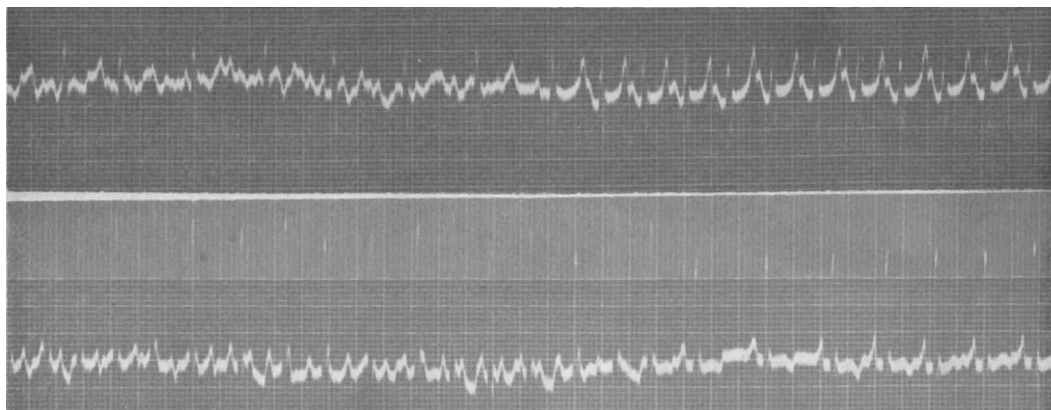


FIG. 1.

Fig. 1a (upper figure) shows the termination of auricular fibrillation and Fig. 1b (lower) the termination of auricular impure flutter by an intravenous injection of fagarine.

TABLE I.
Time of Disappearance of Arrhythmia.

Date	Prevailing arrhythmia	Time of disappearance of arrhythmia, seconds	Remarks
9/30	fibrillation	48	vagi intact
10/7	"	36	" severed
14	flutter	55	" intact
21	fibrillation	12	" severed
11/11	"	25	" "
25	"	18	" intact
1/7	"	25	" severed
2/26	"	22	" "
4/22	flutter	31	" "
5/13	fibrillation	42	" "

is also emphasized because the clinical administration of the drug occasionally leads to serious disturbances of stimulus formation in the ventricle.

The systolic blood pressure showed a temporary rise lasting only 2 to 5 minutes and amounting to 30-40 mm Hg. In all experiments the original values of blood pressure were registered within 5 minutes.

Following the injection of fagarine renewed

subepicardial injection of the aconitine solution had no effect on the existing sinus rhythm for about 45 minutes. After this time it was possible to elicit tachycardias and fibrillation for a second time with this method.

Summary. The intravenous injection of fagarine in dogs with an auricular flutter or fibrillation caused by aconitine abolishes these arrhythmias within one minute and leads to the reappearance of sinus rhythm.